

Alzheimer Drugs Currently Available in the United States

Donepezil (Aricept – Eisai, Aricept ODT – Eisai), Galantamine (Razadyne – Ortho-McNeil Neuro, Razadyne ER – Ortho-McNeil Neuro, generic), Rivastigmine (Exelon – Novartis), Tacrine (Cognex – Sciele)
AHFS 12:04 Parasympathomimetic (Cholinergic) Agents

Memantine (Namenda – Forest)
AHFS 28:92 Central Nervous System Agents, Miscellaneous

The following tables provide a brief comparison of agents for Alzheimer disease currently marketed in the United States. Only single agent products are available for these agents.

Table 1. Brief Comparison of Agents for Alzheimer Disease¹⁻¹⁶

Characteristics	Donepezil	Galantamine	Memantine	Rivastigmine	Tacrine
Brand name(s)	Aricept, Aricept ODT	Razadyne, Razadyne ER	Namenda	Exelon	Cognex
Generic available	Tablets: Yes* ODT: No	Tablets, IR: Yes Oral solution, IR: Yes* Capsules ER: Yes	Tablets: No Oral solution: No	Capsules: Yes* Oral solution: No Transdermal: No	Capsules: No
Latest Patent / Exclusivity Expiration	<ul style="list-style-type: none"> Tablets: March 2019; generics are tentatively approved but not marketed ODT: November 2010 	<ul style="list-style-type: none"> Tablets, IR: expired; generics marketed Oral solution, IR: December 2008; generics tentatively approved but not marketed Capsules, ER: expired; generics marketed 	<ul style="list-style-type: none"> Tablets: April 2010 Oral solution: April 2010 	<ul style="list-style-type: none"> Capsules: February 2014; generics tentatively approved but not yet marketed. Oral solution: February 2014; generics tentatively approved but not marketed Transdermal: January 2019 	<ul style="list-style-type: none"> Capsules: expired; no generics approved.
Dosage form and strengths	<ul style="list-style-type: none"> Tablets: 5 and 10 mg ODT: 5 and 10 mg 	<ul style="list-style-type: none"> Tablets, IR: 4, 8, and 12 mg Oral solution 4 mg/mL, IR: 100 mL Capsules, ER: 8, 16, and 24 mg 	<ul style="list-style-type: none"> Tablets: 5 and 10 mg Oral solution 2 mg/mL: 360 mL 	<ul style="list-style-type: none"> Capsules: 1.5, 3, 4.5, and 6 mg Oral solution 2 mg/mL: 120 mL Transdermal: 4.6 mg/24 hr and 9.5 mg/24 hr 	<ul style="list-style-type: none"> Capsules: 10, 20, 30, and 40 mg
Labeled use	Treatment of mild, moderate, or severe Alzheimer dementia in adults	Treatment of mild or moderate Alzheimer dementia in adults	Treatment of moderate or severe Alzheimer dementia in adults	Treatment of mild or moderate dementia associated with Alzheimer disease or Parkinson disease, in adults	Treatment of mild or moderate Alzheimer dementia in adults

Table 1. Brief Comparison of Agents for Alzheimer Disease (continued)

Characteristics	Donepezil	Galantamine	Memantine	Rivastigmine	Tacrine
Dosage regimen, adults	5 mg/day initially. Gradually titrate to 10 mg/day after 4 – 6 weeks. Give at bedtime.	IR tablets and oral solution: 4 mg BID initially. Gradually titrate to maintenance dose of 16 – 24 mg/day, given in divided doses BID. Capsules, ER: 8 mg once daily initially. Gradually titrate to maintenance dose of 16 – 24 mg once daily.	5 mg/day initially. Gradually titrate to maintenance dose of 20 mg/day, given in divided doses BID.	Capsules and oral solution: 1.5 mg BID initially. Gradually titrate up as needed, to maximum of 6 mg BID. Transdermal: 4.6 mg/24 hours initially. Gradually titrate up as needed to maximum of 9.5 mg/24 hours.	10 mg QID initially. Gradually titrate up as needed to a maximum of 40 mg QID.
Contraindications	Contraindicated in patients with hypersensitivity to the drug or related compounds (piperidine derivatives).	Contraindicated in patients with hypersensitivity to the drug or any ingredients in the product.	Contraindicated in patients with hypersensitivity to the drug or any ingredients in the product.	Contraindicated in patients with hypersensitivity to the drug, other carbamates, or any ingredients in the product.	Contraindicated in patients with hypersensitivity to the drug or acridine derivatives; and in patients with liver toxicity during prior tacrine therapy.
Monitoring Required	None	None	None	Monitor weight; adjust dose if weight loss occurs.	Monitor LFTs at baseline, every other week from week 4 – 16, then every 3 months. If LFTs increase, reduce dose or interrupt therapy and monitor more frequently until LFTs return to normal.
Pharmacology					
Acetylcholinesterase Inhibitor	Yes	Yes	No	Yes	Yes
Butyrylcholinesterase Inhibitor	No	No	No	Yes	Yes
Nicotinic Receptor Modulator	No	Yes	No	No	No
NMDA Receptor Antagonist	No	No	Yes	No	No
Pharmacokinetics					
Bioavailability	100% (tablets and ODT are bioequivalent)	90%	Well-absorbed	36 – 40%	17%, extensive first-pass effect
Time to Peak (hrs)	3 – 4	IR: 1 ER: 4.5 – 5	3 – 7	Oral: 1 Transdermal: 10 – 16	1 – 2

Abbreviations: ER = extended release; IR = immediate release; LFTs = liver function tests; NMDA = N-methyl-D-aspartate; ODT = orally disintegrating tablets.

* Generics are tentatively approved but not yet marketed.

Table 1. Brief Comparison of Agents for Alzheimer Disease (continued)

Characteristics	Donepezil	Galantamine	Memantine	Rivastigmine	Tacrine
Effect of Food on Absorption	None. Give without regard to meals.	IR: Delays peak by 1.5 hours, no effect on extent. Give with meals. ER: None. Give without regard to meals.	None. Give without regard to meals.	Delays peak by 1.5 hours, increases extent 30%. Give with meals.	Reduces extent 30 – 40%. Give on an empty stomach.
Volume of Distribution	12 L/kg	2.5 L/kg	9 – 11 L/kg	1.8 – 2.7 L/kg	4.98 L/kg
Protein Binding	96%, to albumin (75%) and α_1 -acid glycoprotein (21%)	18%	45%	40%	55%
Metabolism	Hepatic: CYP2D6, CYP3A4, glucuronidation	Hepatic: CYP2D6, CYP3A4, glucuronidation	Hepatic: glucuronidation	Hydrolyzed by esterases	Hepatic: CYP1A2
Active Metabolites?	Two active metabolites	None	Minimal	None	Unknown
Excretion	Urine: 17% unchanged, 40% as metabolites Feces: 15%	Urine: 32% unchanged, 12% as metabolites	Urine: 57 – 82% unchanged	Urine: 97% as metabolites Feces: 0.4%	Unknown
Half-Life (hrs)	70	7	60 – 80	1.5	2 – 4
Duration of Effect (hrs)	Unknown	3	Unknown	10	Unknown

Abbreviations: ER = extended release; IR = immediate release; LFTs = liver function tests; NMDA = N-methyl-D-aspartate; ODT = orally disintegrating tablets.

* Generics are tentatively approved but not yet marketed.

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